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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,573	02/08/2001	Etienne Regulier	017753-137	5075

7590 06/20/2003

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	13

DATE MAILED: 06/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,573	REGULIER ET AL.	
	Examin r	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2003* .

2a)☒ This action is **FINAL.** 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-21 and 24-32* is/are pending in the application.

4a) Of the above claim(s) *8-10,16-18 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7,11-15,19,20,24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *16 April 2003* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Final Rejection

Claims 1,7-21, 24-32 are pending.

Applicants' traversal, the cancellation of claims 2-6 and 22-23, the amendment to claims 1, 7, 14, and 24, the addition of claims 25-32 in paper no. 12 filed on 4/16/03 is acknowledged and considered.

The examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be to directed to Brian Whiteman, Art Unit 1635.

Election/Restrictions

This application contains claims 8-10, 16-18 and 21 drawn to an invention nonelected with traverse in Paper No. 8 filed on 11/20/02. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

Applicant's arguments, see paper no. 12, filed 4/16/03, with respect to the objection(s)of claim(s) 24 and 25 have been fully considered and are persuasive. Therefore, the objection has been withdrawn. However, upon further consideration, a new ground(s) of objection is made in view of the amendment to claim 7 and the addition of claim 32.

Claims 7, 19, and 32 are objected to because of the following informalities: Claim 7 reads on non-elected embodiment "all or part of interferon gamma (IFN-γ)."

The statement in claim 19, "**a** composition according to 13, claim 1" is in improper format for a dependent claim. The dependent claim should recite -- **the** composition according to **claim** 13 **or** claim 1 --

The first letter of the word "the" is not capitalized in Claim 32.

Appropriate correction is required.

Applicant's arguments, see paper no. 12, filed on 4/16/03 with respect to 112 first paragraph rejection have been fully considered and are persuasive. The rejection of claims 1-5, 7, 11-15, 19, 20, 23 and 24 has been withdrawn because of the amendment to claims 1, 7, 14, and 24 and the cancellation of claims 2-5 and 23.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 7, 11-15, 19, 20, and 24 remain and claims 26 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557, EFD 2/21/96) taken with Hobart et al. (US Patent 5,147,055, EFD 3/14/97) and Nakashima et al. (Pharm. Res. 13:1896-1901, 1996).

Boursnell teaches virus vectors encoding nucleotide sequences expressing immunomodulating proteins including cytokines and chemokines and combinations thereof (col. 6, lines 55-67), such as IL-2, MIP1α, and MIP1β (col. 7, lines 1-11) for cancer immunotherapy, wherein each of the sequences are placed under control of a known viral promoter or a mammalian specific promoter (col. 9, lines 45-51). Boursnell further teaches making and using a vector comprising two or more nucleotide sequences or a mixture of two vectors containing at least one gene encoding a different immunomodulator product (col. 8, lines 50-55). Furthermore, Boursnell teaches a method of using the vector for cancer immunotherapy in an animal by direct or indirect administration (col. 11, lines 8-67). The vector can be a mutant

DNA or RNA virus, e.g., adenovirus, poxvirus (col. 5, lines 49-55). The vectors used in the method taught by Boursnell are in pharmaceutically acceptable formulas. However, Boursnell does not specifically teach making and using a composition comprising a nucleotide sequence encoding Il-2 and a nucleotide sequence encoding an MIP chemokine for reducing tumors in an animal.

However, at the time the invention was made, Hobart teaches a method of treating a solid tumor in an animal comprising introducing a vector comprising IL-2 into the solid tumors (col. 4, lines 33-41, col. 4, line 66- col. 5, and col. 33, line 33 to col. 36, line 37).

In addition, at the time the invention was made, Nakashima teaches reducing tumorigenicities in mice inoculated with adenocarcinoma cells (page 1896) using a vector comprising a nucleotide sequence encoding MIP1α. Nakashima teaches that MIPα has potential value for cancer gene therapy.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the inventions was made to combine the teaching of Boursnell taken with Hobart and Nakashima to make and use a composition comprising a nucleotide sequence encoding Il-2 and a nucleotide sequence encoding an MIP chemokine for treating a tumor in an animal. One of ordinary skill in the art would have been motivated to combine the teachings because a nucleotide sequence encoding IL-2 and a nucleotide sequence encoding MIP1α were well known to one of ordinary skill in the art for reducing tumors in an animal. Therefore, is would been obvious to one of ordinary skill in the art to use the composition to reduce tumors in an animal and achieve a reasonable expectation of success.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicants' arguments filed 4/16/03 have been fully considered but they are not persuasive. MPEP 2144.06 states, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). This is the case here. At the time the invention was made, a vector comprising a nucleotide sequence encoding a MIP chemokine or a vector comprising a nucleotide sequence encoding IL-2 were known to treat a tumor in an animal. In addition, Boursnell teaches the reasonable expectation of success for making a composition comprising a nucleotide sequence encoding immunomodulating proteins.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., direct administration of vectors expressing both a MIP chemokines and IL-2 can synergistically work to successfully inhibit in vivo tumor growth) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 1, 11, 13, 14, 15, and 25-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557, EFD 2/21/96) taken with Hobart et al.

(US Patent 5,147,055, EFD 3/14/97) and Nakashima et al. (Pharm. Res. 13:1896-1901, 1996) in further view of Bruder et al. (US Patent 6,440,944, EFD 10/16/98).

The rejection of the base claims 1, 11, 13, 14, 15, and 26 under 35 U.S.C. 103(a) are applied here as indicated above, by Boursnell taken with Hobart and Nakashima. However, Boursnell taken with Hobart and Nakashima do not specifically teach making a replication defective adenoviral vector, wherein said adenoviral vector is deleted in the E1 region, or E1 and E4, or E1 and E3, or E1, E3, and E4.

However, at the time the invention was made, replication defective adenoviral vectors were well known in the art for gene delivery because they are superior vehicle for transferring genetic material to a wide variety of cells and represent a safe choice of gene transfer. Bruder teaches that a variety of recombinant adenoviral vectors are known in the art for gene delivery (col. 1, lines 34-55). Bruder teaches an adenoviral vector with a gene of interest inserted into the E1 region of the adenovirus. Furthermore, Bruder teaches multiply deficient adenoviral vectors that are deficient in E1, E3 and E4. One of ordinary skill in the art understands that a recombinant adenoviral vector is replication defective because genes essential for adenovirus replication are deleted.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to make and use a replication defective adenoviral vector in the composition taught by Boursnell taken with Hobart and Nakashima. One of ordinary skill in the art would have been motivated to use a replication defective adenoviral vector because they are superior vehicle for transferring genetic material to a wide variety of cells and represent a safe

choice of gene transfer. In addition, one of ordinary skill in the art would have been motivated to use a multiply deficient adenoviral vector to abolish expression of adenoviral proteins.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1, 11, 13, 14, 15, and 25-30 have been considered but are moot in view of the reasons set forth in the prior 103(a) rejection and the new ground(s) of rejection.

Claims 14, 15, 31, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boursnell et al. (US Patent 6,287,557, EFD 2/21/96) taken with Hobart et al. (US Patent 5,147,055, EFD 3/14/97) and Nakashima et al. (Pharm. Res. 13:1896-1901, 1996) in further view of Gruber (US Patent 6,410,326, EFD 6/7/1995).

The rejection of the base claims 14, 15, and 31 under 35 U.S.C. 103(a) are applied here as indicated above, by Boursnell taken with Hobart and Nakashima. However, Boursnell taken with Hobart and Nakashima do not specifically teach making a poxvirus vector selected from the group consisting of vaccinia virus, MVA, and canary pox.

However, at the time the invention was made, vaccinia virus were well known in the art for expressing heterologous proteins at high levels as taught by Gruber (col. 7, line 65, col.8, line26).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to make and use vaccinia virus in the composition taught by Boursnell taken with Hobart and Nakashima. One of ordinary skill in the art would have been motivated to

make and use a vaccinia viral vector because vaccinia virus vectors were well known in the art for expressing heterologous proteins at high levels.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 14, 15, 31, and 32 have been considered but are moot in view of the reasons set forth above in the first 103(a) rejection and in view of the new ground(s) of rejection.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe

Brian Whiteman
Patent Examiner, Group 1635

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER